

(b) The neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity.

(d) The batch for bacitracin content, neomycin content, polymyxin B content, and moisture.

(ii) Samples required:

(a) The bacitracin used in making the batch: 10 packages, each containing approximately 1.0 gram.

(b) The neomycin sulfate used in making the batch: 10 packages, each containing approximately 1.0 gram.

(c) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 1.0 gram.

(d) The batch: A minimum of 7 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Bacitracin content*. Proceed as directed for bacitracin zinc in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 1. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 1. Remove an aliquot, add sufficient hydrochloric acid so that the amount of acid in the final solution will be the same as in the reference concentration of the working standard and further dilute with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(ii) *Neomycin content*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 0.1M potassium phosphate buffer, pH 8.0 (solution 3), and shake

well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 3. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 3. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(iii) *Polymyxin B content*. Proceed as directed in § 436.105 of this chapter, except add to each concentration of the polymyxin B standard response line a quantity of neomycin to yield the same concentration of neomycin as that present when the sample is diluted to contain 10 units of polymyxin B per milliliter. Prepare the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 10 percent potassium phosphate buffer, pH 6.0 (solution 6), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 6. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 6. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(2) *Moisture*. Proceed as directed in § 436.201 of this chapter.

[42 FR 27233, May 27, 1977, as amended at 50 FR 19920, May 13, 1985]

§ 448.510f Bacitracin-polymyxin B sulfate topical aerosol.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Bacitracin-polymyxin B sulfate topical aerosol is bacitracin and polymyxin B sulfate in a suitable and harmless vehicle, packaged in a pressurized container with a suitable and harmless inert gas. Each gram contains 500 units of bacitracin and 5,000 units of polymyxin B. It may contain a suitable local anesthetic. Its bacitracin content is satisfactory if it is not less than 90 percent and not more than 130 percent

of the number of units of bacitracin that it is represented to contain. Its polymyxin B content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of polymyxin B that it is represented to contain. Its moisture content is not more than 0.5 percent. The bacitracin used conforms to the standards prescribed by § 448.10(a)(1). The polymyxin B sulfate used conforms to the standards prescribed by § 448.30(a)(1).

(2) *Labeling.* (i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark;

(b) The name and quantity of each active ingredient contained in the drug; and

(c) An expiration date that conforms to the requirements prescribed by § 432.5(a)(3) of this chapter.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions under which the layman can use the drug safely and efficaciously.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The bacitracin used in making the batch for potency, loss on drying, pH, and identity.

(b) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(a) The bacitracin used in making the batch: 10 packages, each containing approximately 1.0 gram.

(b) The polymyxin B sulfate used in making the batch: 10 packages, each containing 1.0 gram.

(c) The batch: A minimum of 12 immediate containers.

(b) *Tests and methods of assay.* The container must remain inverted throughout the sampling procedure. Freeze the container overnight at -70°C . Remove from the freezer and puncture the container to allow the propellant to dissipate. Open the container, mix well, and proceed as described in

paragraphs (b) (1) and (2) of this section.

(1) *Potency*—(i) *Bacitracin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample from the container into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 1. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 1. Remove an aliquot, add sufficient hydrochloric acid so that the amount of acid in the final solution will be the same as in the reference concentration of the working standard, and further dilute with solution 1 to the reference concentration of 1.0 unit of bacitracin per milliliter (estimated).

(ii) *Polymyxin B content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed portion of the sample from the container into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 10 percent potassium phosphate buffer, pH 6.0 (solution 6), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 6. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 6. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

(2) *Moisture.* Proceed as directed § 436.201 of this chapter, using the titration procedure and calculation in paragraph (e)(3) of that section and 1- to 2-milliliter portions of the sample from the container.

[51 FR 35212, Oct. 2, 1986, as amended at 55 FR 9722, Mar. 15, 1990; 55 FR 11584, Mar. 29, 1990]